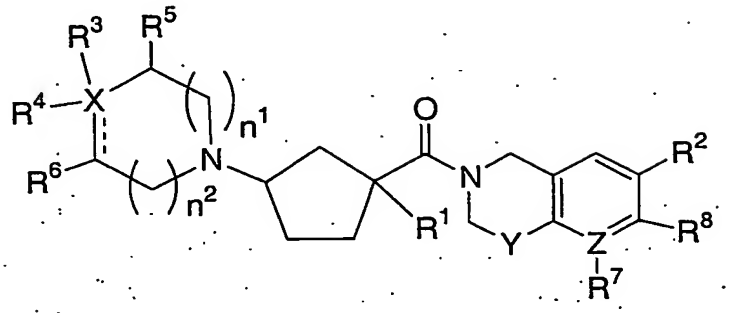
WHAT IS CLAIMED IS:

1. A compound represented by formula I:



I

or a pharmaceutically acceptable salt thereof, or an individual diastereomer thereof, wherein:

X is C, N, O or S;

Y is O, S, SO, SO_2, or NR^9;

Z is C or N;

R^1 is hydrogen, -C_{0-6}alkyl-W-(C_{1-6}alkyl)-, -(C_{0-6}alkyl)-W-(C_{0-6}alkyl)-(C_{3-7}cycloalkyl)-(C_{0-6}alkyl), -(C_{0-6}alkyl)-W-phenyl, or -(C_{0-6}alkyl)-W-heterocycle, wherein the alkyl, phenyl, heterocycle and the cycloalkyl are optionally substituted with 1-7 independent halo, hydroxy, -O-C_{1-3}alkyl, trifluoromethyl, C_{1-3}alkyl, -O-C_{1-3}alkyl, -CO_2R^{10}, -CN, -$NR^{10}R^{10}$, -$NR^{10}COR^{10}$, -$NR^{10}SO_2R^{11}$, or -$CONR^{10}R^{10}$ substituents;

W is a single bond, -O-, -S-, -SO-, -SO_2-, -CO-, -CO_2-, -$CONR^{10}$- or -NR^9-;

R^2 is -halo, -C_{0-6}alkyl, C_{0-6}alkyl-W-C_{1-6}alkyl, C_{0-6}alkyl-W-C_{3-7}cycloalkyl, C_{0-6}alkyl-W-phenyl, or C_{0-6}alkyl-W-heterocycle, wherein the C_{1-6}alkyl, C_{3-7}cycloalkyl, phenyl and heterocycle optionally are independently substituted with 1-6 halo, trifluoromethyl, -CN, -C_{1-6}alkyl, or hydroxy substituents;

R^3 is hydrogen, -(C_{0-6}alkyl)-phenyl, -(C_{0-6}alkyl)-heterocycle, -(C_{0-6}alkyl)-C_{3-7}cycloalkyl, -(C_{0-6}alkyl)-CO_2R^{10}, -(C_{0-6}alkyl)-(alkene)-CO_2R^{10} (C_{0-6}alkyl)-SO_3H, -(C_{0-6}alkyl)-W-C_{0-4}alkyl, -(C_{0-6}alkyl)-$CONR^{10}$-phenyl, or -(C_{0-6}alkyl)-$CONR^{12}$-V-CO_2R^{10}, and wherein R^3 is nothing when X is O, and wherein C_{0-6}alkyl is optionally substituted with 1-5 independent halo, hydroxy, -C_{0-6}alkyl, -O-C_{1-3}alkyl, trifluoromethyl, or -C_{0-2}alkyl-phenyl substituents, and wherein the phenyl, heterocycle, cycloalkyl, and C_{0-4}alkyl is optionally substituted with 1-5 independent halo, trifluoromethyl, hydroxy, C_{1-3}alkyl, -O-C_{1-3}alkyl, -C_{0-3}-CO_2R^{10}, -CN, -$NR^{10}R^{10}$, -$CONR^{10}R^{10}$, or -C_{0-3}-heterocycle substituents, and wherein the phenyl and heterocycle may be fused to another heterocycle, which itself optionally may be substituted with 1-2 independently hydroxy, halo, -CO2R10,

or –C1-3alkyl substituents, and where alkene is optionally substituted with 1-3 independently halo, trifluoromethyl, C_{1-3}alkyl, phenyl, or heterocycle substituents;

V is C_{1-6}alkyl or phenyl;

R^{12} is hydrogen, C_{1-4}alkyl, or R^{12} is joined via a 1-5 carbon tether to one of the carbons of V to form a ring;

R^4 is nothing when X is either O, or N or when a double bond joins the carbons to which R^3 and R^6 are attached, or R^4 is hydroxy, C_{1-6}alkyl, C_{1-6}alkyl-hydroxy, -O-C_{1-3}alkyl, -CO_2R^{10}, -$CONR^{10}R^{10}$, or -CN;

or R^3 and R^4 are joined together to form a 1H-indenyl, 2,3-dihydro-1H-indenyl, 2,3-dihydro-benzofuranyl, 1,3-dihydro-isobenzofuranyl, 2,3-dihydro-benzothiofuranyl, 1,3-dihydro-isobenzothiofuranyl, 6*H*-cyclopenta[*d*]isoxazol-3-olyl, cyclopentanyl, or cyclohexanyl ring, wherein the ring formed optionally is substituted with 1-5 independently halo, trifluoromethyl, hydroxy, C_{1-3}alkyl, -O-C_{1-3}alkyl, -C_{0-3}-CO_2R^{10}, -CN, -$NR^{10}R^{10}$, -$CONR^{10}R^{10}$, or -C_{0-3}-heterocyclyl substituents;

or R^3 and R^5 or R^4 and R^6 are joined together to form a phenyl or heterocyclyl ring, wherein the ring is optionally substituted with 1-7 independent halo, trifluoromethyl, hydroxy, C_{1-3}alkyl, -O-C_{1-3}alkyl, -CO_2R^{10}, -CN, -$NR^{10}R^{10}$, or -$CONR^{10}R^{10}$ substituents;

R^5 and R^6 are independently hydrogen, hydroxy, C_{1-6}alkyl, C_{1-6}alkyl-CO_2R^{10}, C_{1-6}alkyl-hydroxy, -O-C_{1-3}alkyl, or halo, or =O, when R^5 or R^6 is connected to the ring via a double bond;

when Z = C, R^7 is hydrogen, hydroxy, halo, C_{1-6}alkyl optionally substituted with 1-6 fluro, -O-C_{1-6}alkyl optionally substituted with 1-6 fluro, -$NR^{10}R^{10}$, -$NR^{10}CO_2R^{11}$, -$NR^{10}CONR^{10}R^{10}$, -NR^{10}-SO_2-$NR^{10}R^{10}$, -NR^{10}-SO_2-R^{11}, heterocycle, -CN, -$CONR^{10}R^{10}$, -CO_2R^{10}, -NO_2, -S-R^{10}, -SO-R^{11}, -SO_2-R^{11}, or -SO_2-$NR^{11}R^{11}$;

when Z = N, R^7 is nothing or oxide (resulting in a pyridine N-oxide);

R^8 is hydrogen, C_{1-6}alkyl, trifluoromethyl, trifluoromethoxy, chloro, fluoro, bromo, or phenyl;

R^9 is SO_2R^{11}, COR^{10}, $CONHR^{10}$, CO_2R^{11}, or SO_2NHR^{10};

R^{10} is hydrogen, -C_{1-6} alkyl, benzyl, phenyl, or -C_{0-6} alkyl-C_{3-6} cycloalkyl, optionally substituted with 1-3 independent halo, C_{1-3}alkyl, C_{1-3}alkoxy or trifluoromethyl substituents;

R^{11} is C_{1-6}alkyl, -C_{0-6}alkyl-C_{3-6}cycloalkyl, benzyl or phenyl, optionally substituted with 1-3 independent halo, C_{1-3}alkyl, C_{1-3}alkoxy or trifluoromethyl substitutents;

n^1 and n^2 are independently 0, 1 or 2, wherein the sum of n^1 and n^2 is 0, 1, 2, or 3; and

the dashed line represents a single or a double bond.

2. The compound of Claim 1, wherein X is C.

3. The compound of Claim 1, wherein X is O.

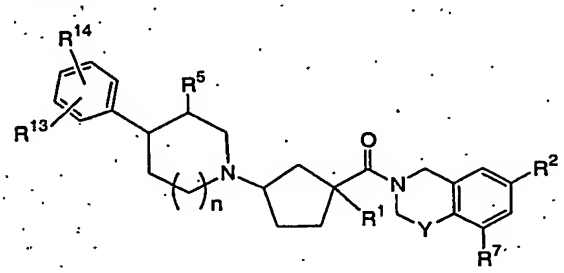
4. The compound of Claim 1, wherein X is N.

5. The compound of Claim 1, wherein

R^3 and R^4 are joined together to form a 1H-indenyl, 2,3-dihydro-1H-indenyl, 2,3-dihydro-benzofuranyl, 1,3-dihydro-isobenzofuranyl, 2,3-dihydro-benzothiofuranyl, 1,3-dihydro-isobenzothiofuranyl, 6*H*-cyclopenta[*d*]isoxazol-3-olyl, cyclopentanyl, or cyclohexanyl ring, wherein the ring formed optionally is substituted with 1-5 independently halo, trifluoromethyl, hydroxy, C_{1-3}alkyl, -O-C_{1-3}alkyl, -C_{0-3}-CO_2R^{10}, -CN, -$NR^{10}R^{10}$, -$CONR^{10}R^{10}$, or -C_{0-3}-heterocyclyl substituents;

or R^3 and R^5 or R^4 and R^6 are joined together to form a phenyl or heterocyclyl ring, wherein the ring is optionally substituted with 1-7 independent halo, trifluoromethyl, hydroxy, C_{1-3}alkyl, -O-C_{1-3}alkyl, -CO_2R^{10}, -CN, -$NR^{10}R^{10}$, or -$CONR^{10}R^{10}$ substituents.

6. The compound of Claim 1, represented by formula Ia:



(Ia)

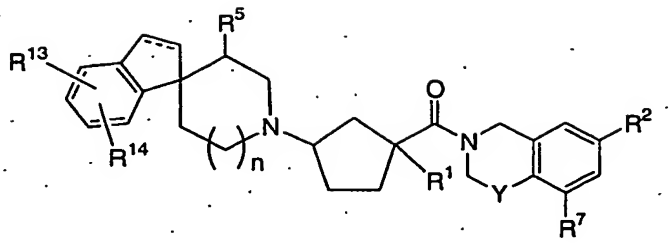
or pharmaceutically acceptable salts and individual diastereomers thereof, wherein R^1, R^2, R^5, R^7, and Y are defined as in Claim 1;

wherein R^{13} and R^{14} are independently hydrogen, halo, trifluoromethyl, hydroxy, -C_{1-3}alkyl, -O-C_{1-3}alkyl, -C_{0-3}-CO_2H, -C_{0-3}-CO_2C_{1-3}alkyl, -CN, or -C_{0-3}-heterocycle;

or R^{13} and R^{14} are joined together to form a heterocycle which is fused to the phenyl ring, and which itself may be unsubstituted or substituted with 1-2 independent hydroxy, halo, -CO_2R^{10}, or –C_{1-3}alkyl substituents; and

n is 0, 1, or 2.

7. The compound of Claim 1, represented by formula Ib:



(Ib)

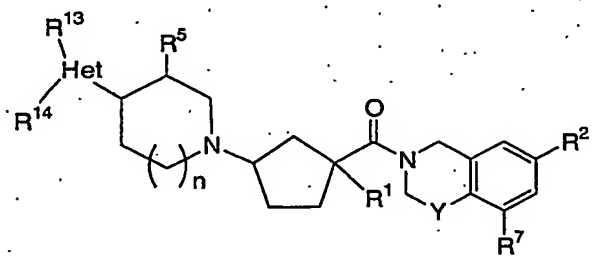
or pharmaceutically acceptable salts and individual diastereomers thereof, wherein R^1, R^2, R^5, R^7, and Y are defined as in Claim 1;

R^{13} and R^{14} are independently hydrogen, halo, trifluoromethyl, hydroxy, -C_{1-3}alkyl, -O-C_{1-3}alkyl, -C_{0-3}-CO_2H, -C_{0-3}-CO_2C_{1-3}alkyl, -CN, or -C_{0-3}-heterocycle;

or R^{13} and R^{14} are joined together to form a heterocycle which is fused to the phenyl ring, and which itself may be unsubstituted or substituted with 1-2 independent hydroxy, halo, -CO_2R^{10}, or -C_{1-3}alkyl substituents; and

n is 0, 1, or 2.

8. The compound of Claim 1, represented by formula Ic:



(Ic)

or pharmaceutically acceptable salts and individual diastereomers thereof, wherein R^1, R^2, R^5, R^7, and Y are defined as in Claim 1;

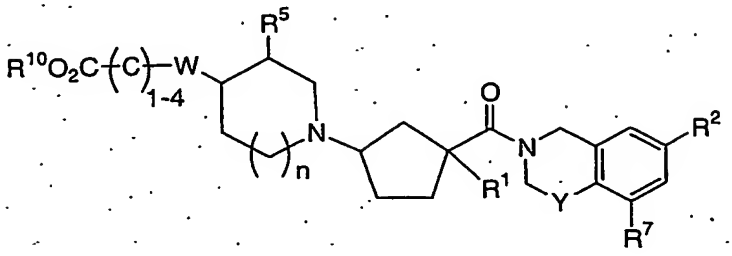
wherein R^{13} and R^{14} are independently hydrogen, halo, trifluoromethyl, hydroxy, -C_{1-3}alkyl, -O-C_{1-3}alkyl, -C_{0-3}-CO_2H, -C_{0-3}-CO_2C_{1-3}alkyl, -CN, or -C_{0-3}-heterocycle;

or R^{13} and R^{14} are joined together to form a heterocycle which is fused to the phenyl ring, and which itself may be unsubstituted or substituted with 1-2 independent hydroxy, halo, -CO_2R^{10}, or -C_{1-3}alkyl substituents;

n is 0, 1, or 2; and

Het is a heterocycle.

9. The compound of Claim 1, represented by formula Id:



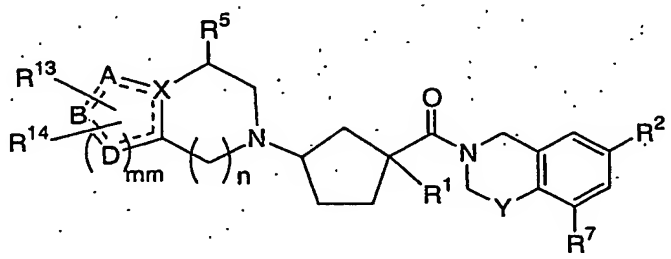
(Id)

or pharmaceutically acceptable salts and individual diastereomers thereof, wherein R^1, R^2, R^5, R^7, R^{10}, Y, and W are as defined in Claim 1;

n is 0, 1, or 2; and

C_{1-4} carbon chain is optionally substituted with 1-4 independent halo, hydroxy, -C_{0-6}alkyl, -O-C_{1-3}alkyl, trifluoromethyl, or -C_{0-2}alkyl-phenyl substituents; or the C_{1-4} carbon chain is part of a C_{3-7}cycloalkyl ring.

10. The compound of Claim 1, represented by formula Ie:



(Ie)

or pharmaceutically acceptable salts and individual diastereomers thereof, wherein R^1, R^2, R^5, R^7, R^{13}, R^{14}, X, and Y are as defined in Claim 1;

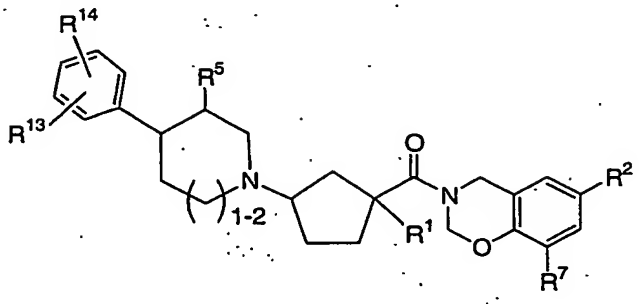
n is 0, 1, or 2;

the dotted lines represent an optional bond;

mm is 1 or 2, and

A, B, and D are each independently C, N, O, or S; or A, B, and D, in combination with mm = 2, form a phenyl ring; or in combination form a heterocycle when at least one of X, A, B, D is N, O, or S.

11. The compound of Claim 1, represented by formula If:

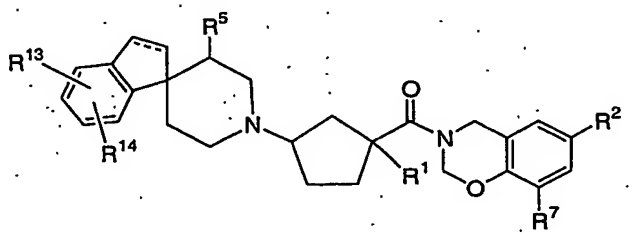


(If)

or pharmaceutically acceptable salts and individual diastereomers thereof, wherein R^1, R^2, R^5, R^7, R^{13}, and R^{14}, are as defined for Claim 1;

or wherein R^{13} and R^{14} are joined together to form a heterocycle fused to the phenyl ring, and wherein the heterocycle is itself is optionally substituted with 1-2 independent hydroxy, halo, $-CO_2R^{10}$, or $-C_{1-3}$alkyl substituents.

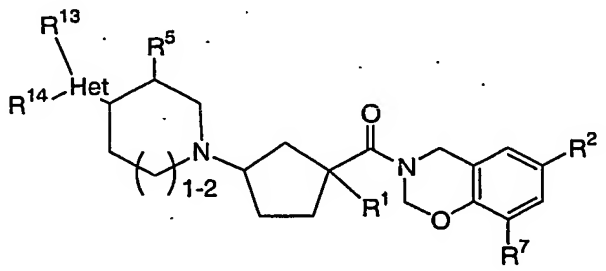
12. The compound of Claim 1, represented by formula Ig:



(Ig)

or pharmaceutically acceptable salts and individual diastereomers thereof, wherein the dashed line represents an optional bond and R^1, R^2, R^5, R^7, R^{13}, and R^{14} are as defined in Claim 1.

13. The compound of Claim 1, represented by formula Ih:

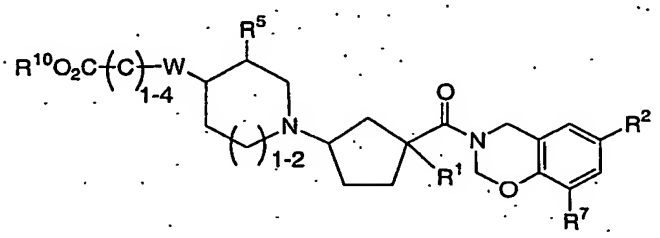


(Ih)

or pharmaceutically acceptable salts and individual diastereomers thereof, wherein R^1, R^2, R^5, R^7, R^{13}, and R^{14} are as defined in Claim 1; and

Het is a heterocycle.

14. The compound of Claim 1, represented by formula Ii:

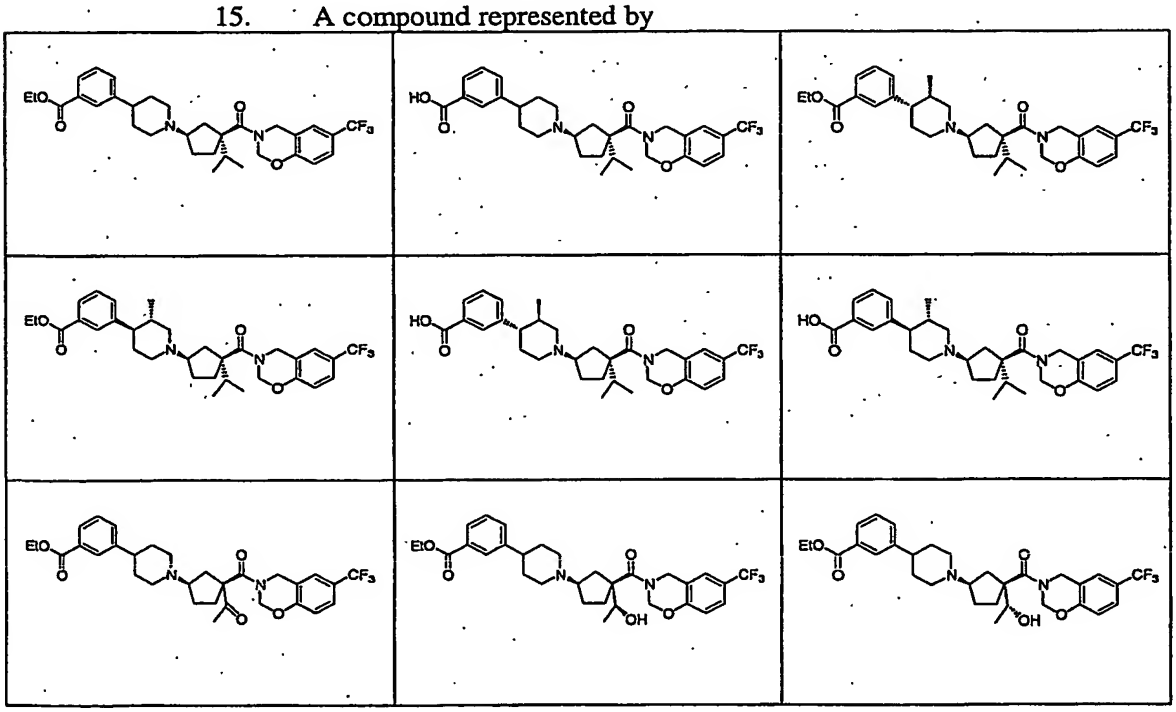


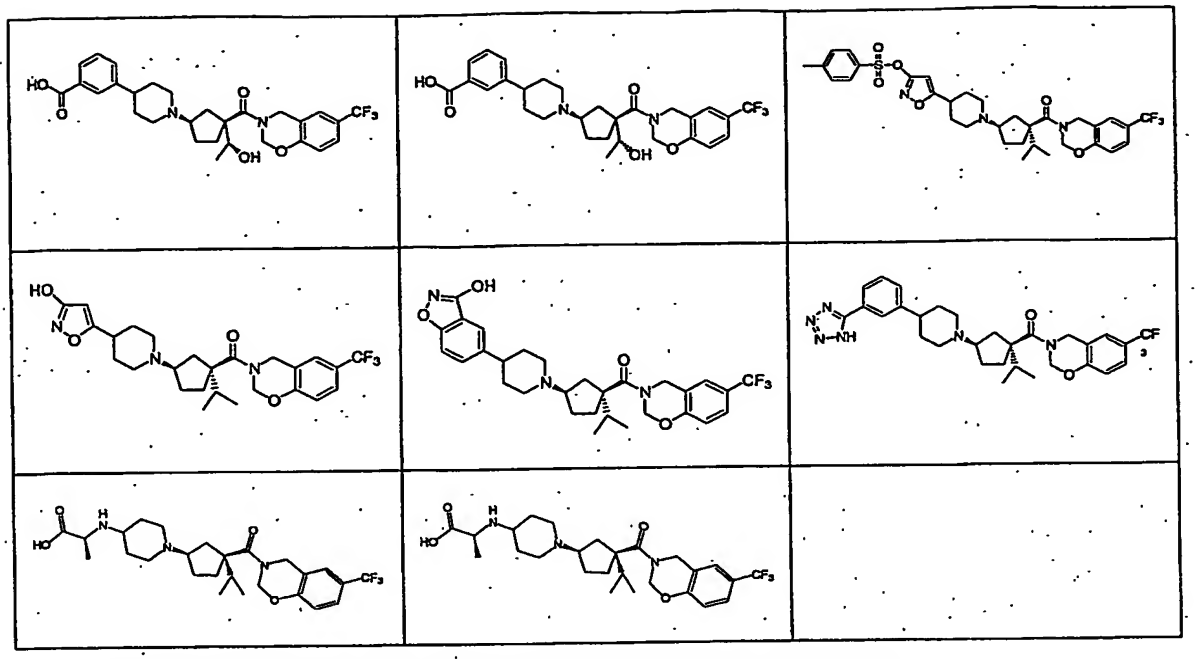
(Ii)

or pharmaceutically acceptable salts and individual diastereomers thereof, wherein R^1, R^2, R^5, R^7, R^{10}, and W are defined as in Claim 1; and

wherein the C_{1-4} carbon chain is optionally substituted with 1-4 independent halo, hydroxy, -C_{0-6}alkyl, -O-C_{1-3}alkyl, trifluoromethyl, or -C_{0-2}alkyl-phenyl substituents.

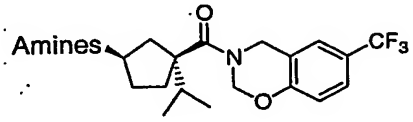
15. A compound represented by



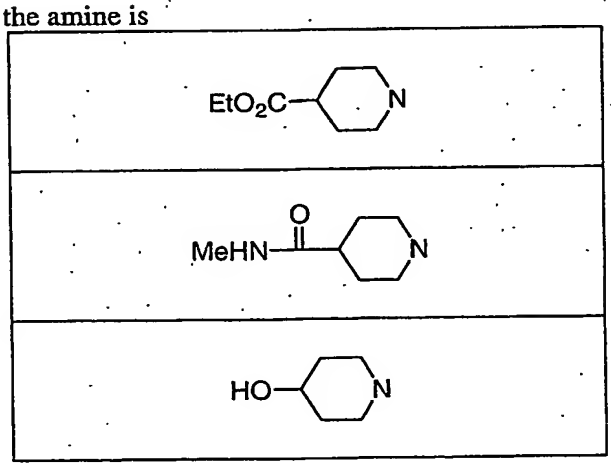


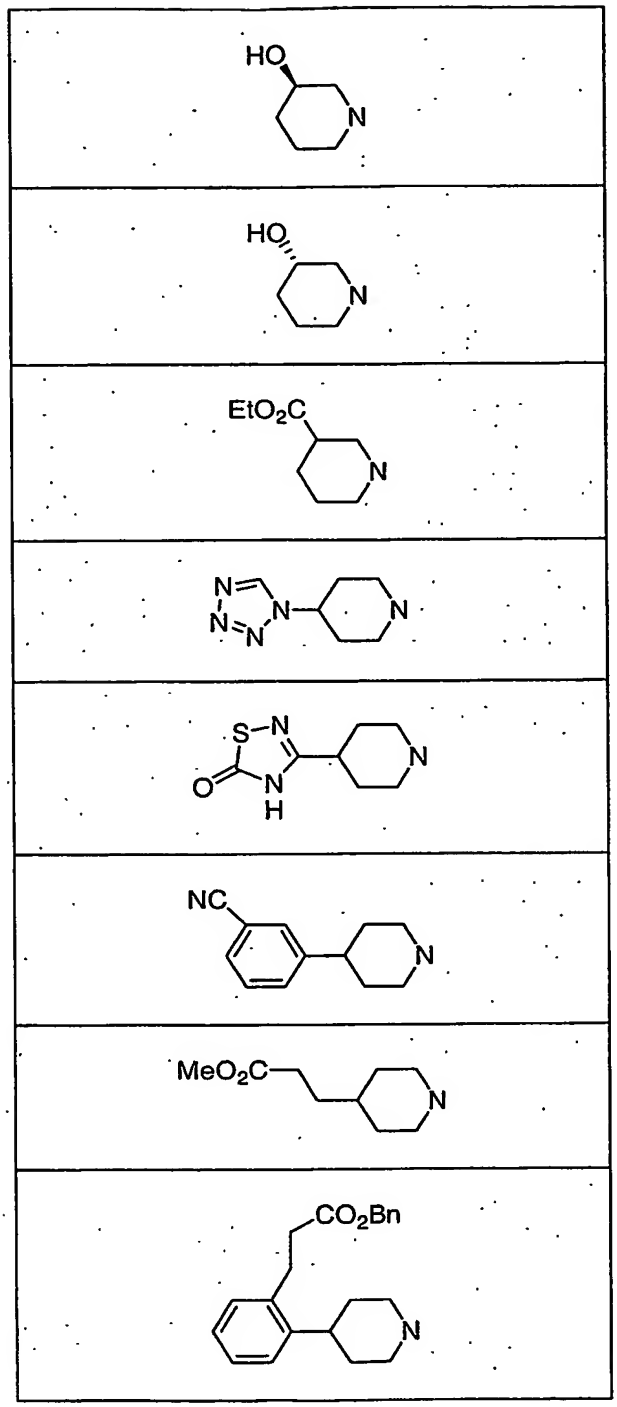
or a pharmaceutically acceptable salt or individual diastereomer thereof.

16. A compound represented by



wherein the amine is




HO
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HO
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EtO2C
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N
N
S
N
O
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H
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NC
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MeO2C
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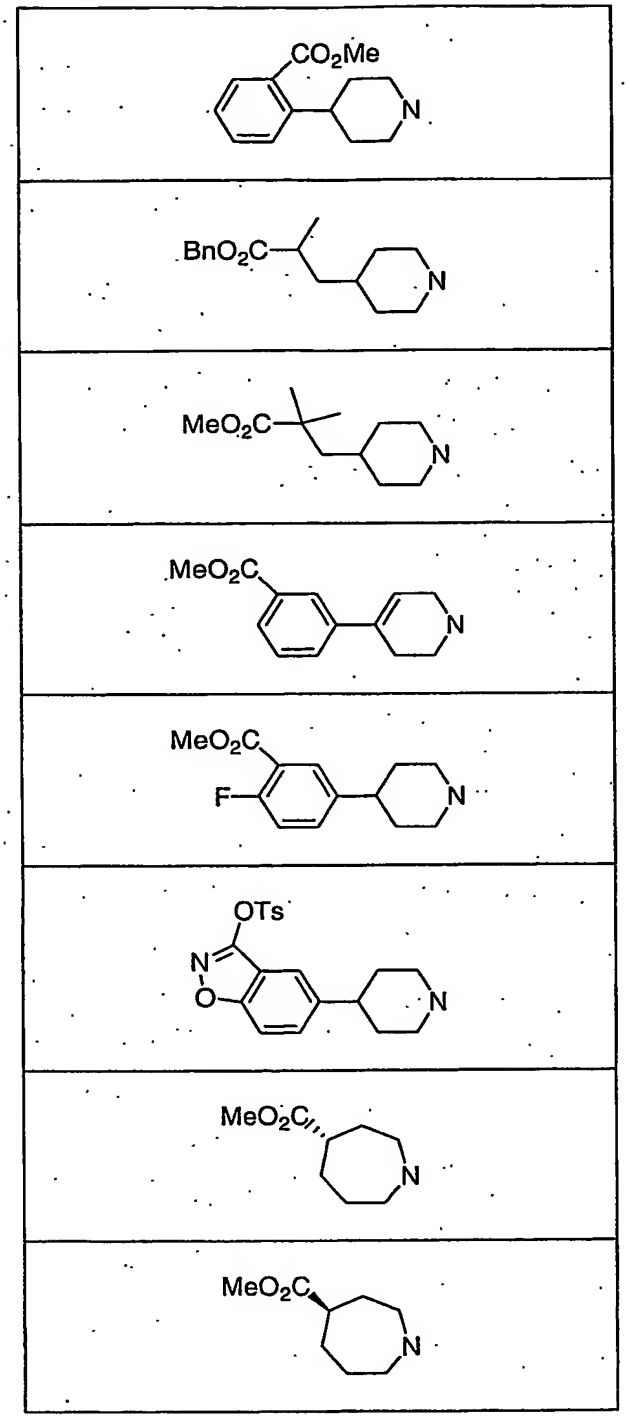
CO2Bn
N


CO2Me
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BnO2C
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MeO2C
F
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OTs
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O
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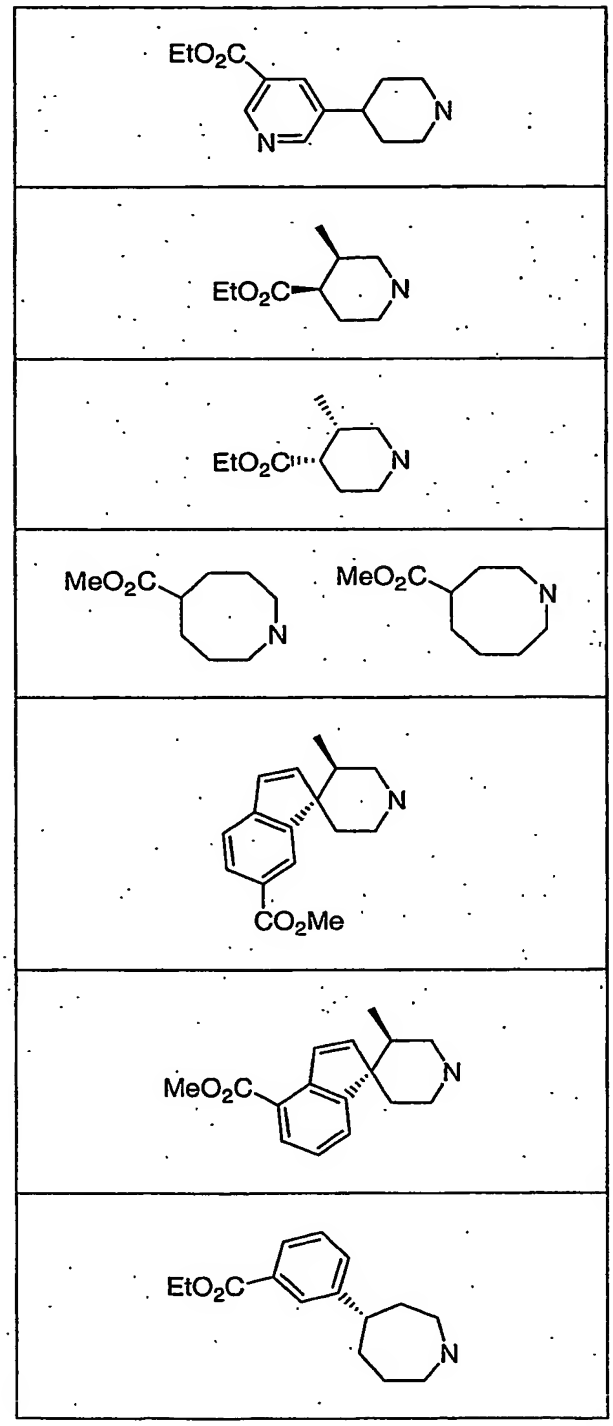
MeO2C
N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CO2Me
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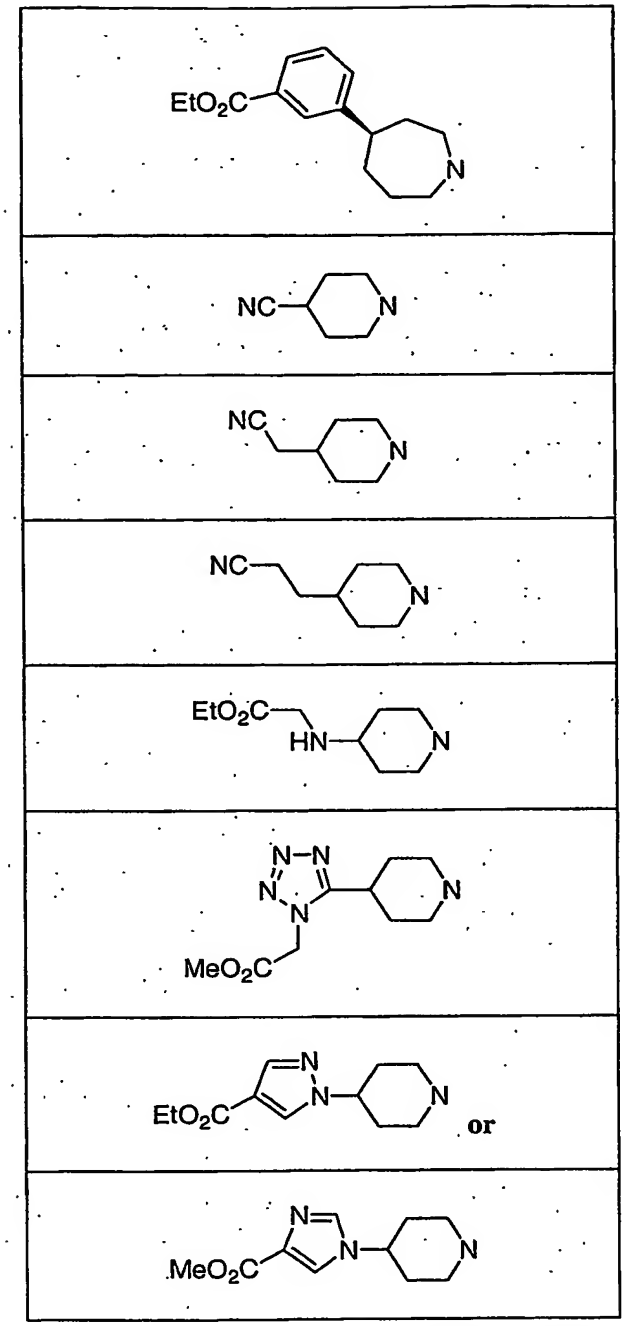
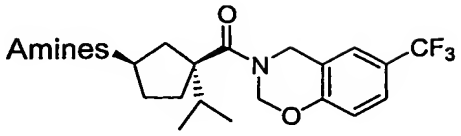
EtO2C
N

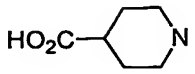
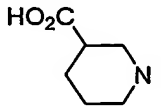
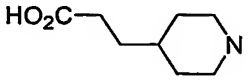
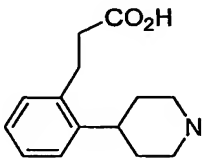
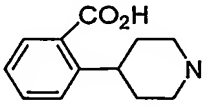
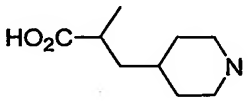
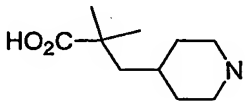


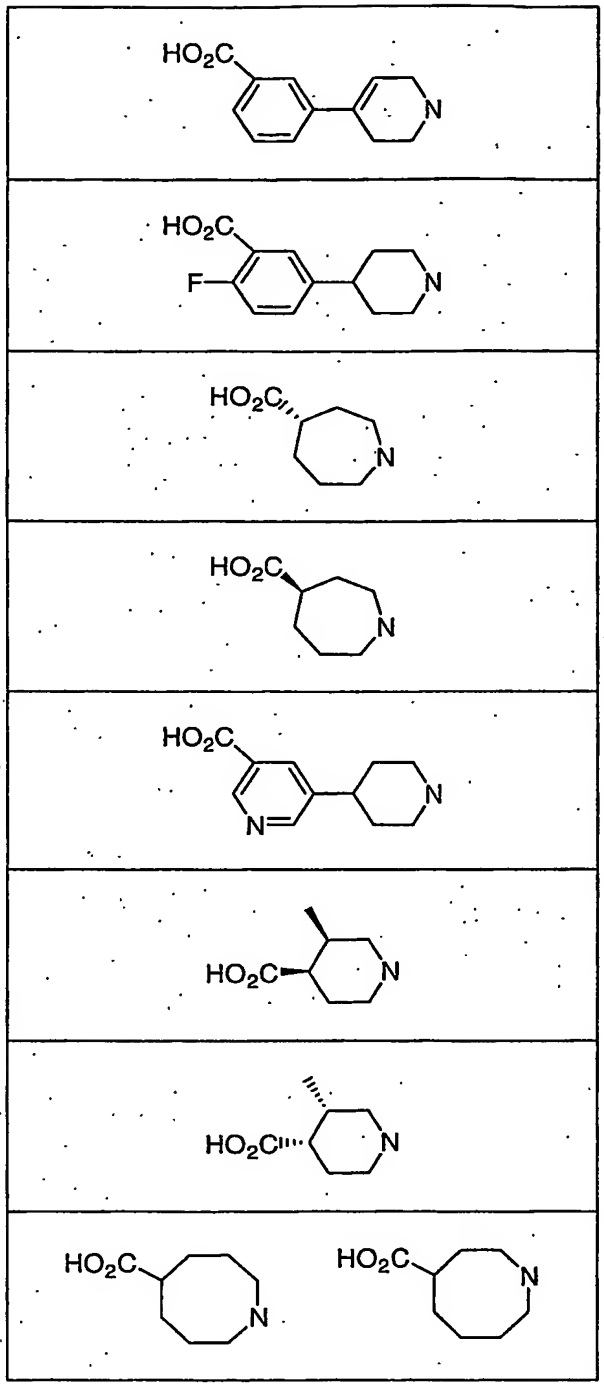
or a pharmaceutically acceptable salt or individual diastereomer thereof.

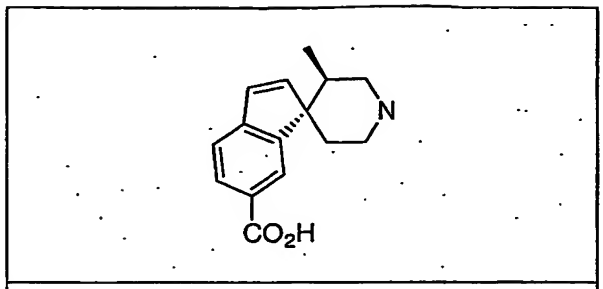
17. A compound represented by

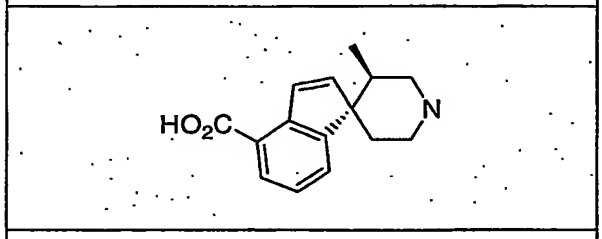


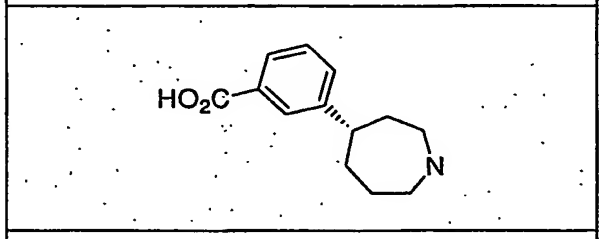
wherein amine is

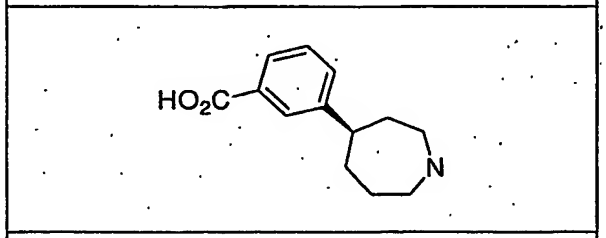








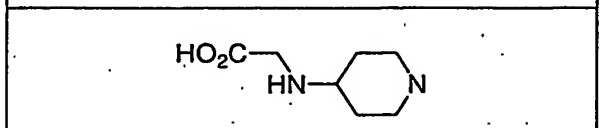


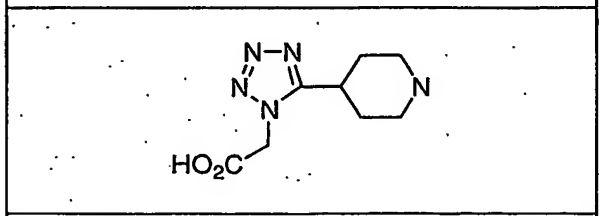


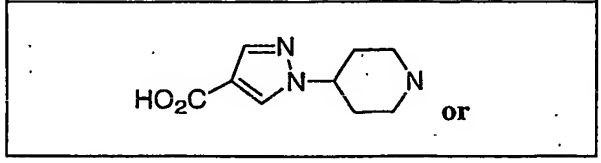




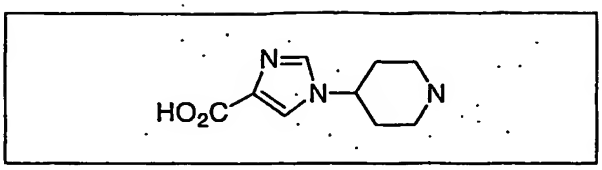






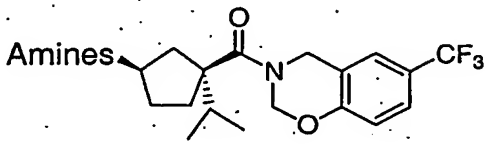


or

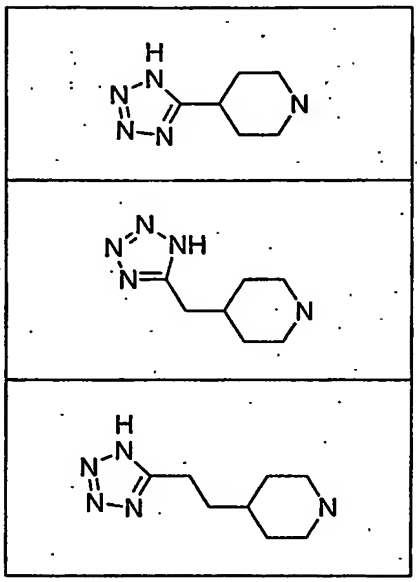


or a pharmaceutically acceptable salt or individual diastereomer thereof.

18. A compound represented by

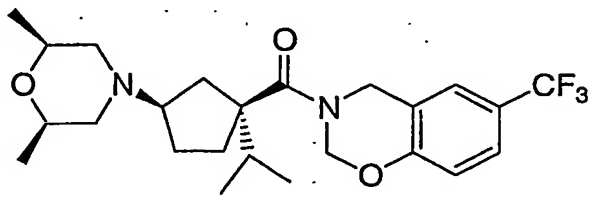


wherein amine is



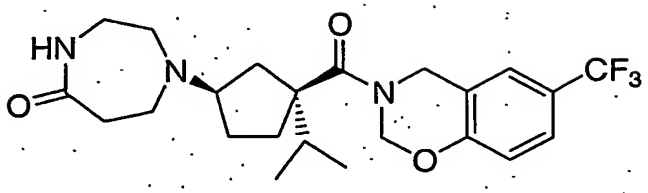
or a pharmaceutically acceptable salt or individual diastereomer thereof.

19. A compound represented by



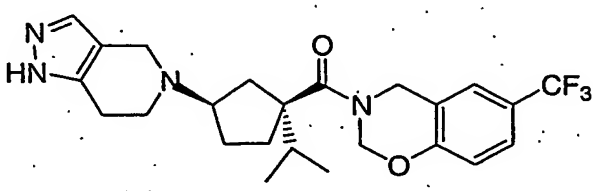
or a pharmaceutically acceptable salt or individual diastereomer thereof.

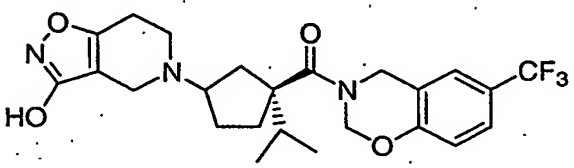
20. A compound represented by

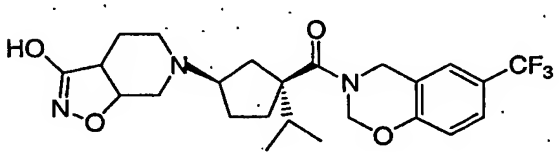


or a pharmaceutically acceptable salt or individual diastereomer thereof.

21. A compound represented by







or a pharmaceutically acceptable salt or individual diastereomer thereof.

22. A pharmaceutical composition which comprises an inert carrier and a compound of Claim 1.

23. A method for modulation of chemokine receptor activity in a mammal which comprises the administration of an effective amount of the compound of Claim 1.

24. A method for treating, ameliorating, controlling or reducing the risk of an inflammatory and immunoregulatory disorder or disease which comprises the administration to a patient of an effective amount of the compound of Claim 1.

25. A method for treating, ameliorating, controlling or reducing the risk of rheumatoid arthritis which comprises the administration to a patient of an effective amount of the compound of Claim 1.